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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,744	07/13/2001	Brian Paul Chadwick	28110/36120A	6794

7590 01/13/2003

LI-HSIEN RIN- LAURES
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EXAMINER
DECLOUX, AMY M

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTOL-90A (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/905,744	CHADWICK ET AL.	
	Examiner	Art Unit	
	Amy M. DeCloux	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *19* is/are allowed.

6)☒ Claim(s) *20-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice to Comoply with Requirements for Sequence Disclosures.

DETAILED ACTION

Claims 19-24 are pending and are under consideration.

Election/Restrictions

Applicant's amendment filed 11-1-02 (Paper No. 10) is acknowledged. In view of said amendment the restriction requirement filed 10-1-02 (Paper No. 8) has been withdrawn.

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). Specifically a reference to Application Number 09/240,639, now US Patent 6350447, is required.

Sequence compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Sequences are disclosed throughout the specification, which lack SEQ ID NO: tags, including in page 95, lines 28-29, page 98, line 26, page 100, lines 27, 28, 30 and 33, page 101, lines 1, 18, 19 and 25, and page 103, lines 7-8. Applicants are required to resubmit a substitute disk and paper copy of the sequences according to the attached "Notice to Comply with the Sequence Rules." Applicant is reminded of the sequence rules which require a submission for all sequences of more than 9 nucleotides or 3 amino acids (see 37 C.F.R. 1.821-1.825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01. Specifically, hyperlinks are disclosed on page 99, lines 19 and 28-29, and on page 100, lines 19-20 and 22. Applicant is

requested to carefully review the submitted specification for any and all embedded hyperlinks and/or other form of browser-executable code.

The abstract of the disclosure is objected to because the word "novel" is stated in line 1 of the Abstract. Patents are presumed to be novel. Correction is required. See MPEP § 608.01(b).

Claim Objections

Claim 24 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Specifically Claim 24 encompasses a broader breadth of proteins compared to that of Claim 19.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

A) Claims 22 and 23-24 are indefinite in their recitation of the phrase "hybridizes under highly stringent conditions" in lines 2-3 of claim 22, because the stringent conditions are disclosed in exemplary terms only on page 11 of the instant specification. Incorporating a specific set of hybridization conditions into the instant claims would overcome this rejection.

B) Claims 20 and 23 are indefinite in their recitation of the phrase "enzymatically active" recited in claim 20, because of the open-end ness of the term enzymatic activity. Incorporating the specific enzymatic activity of phosphohydrolase activity would overcome this rejection.

C) Claims 21 and 23 are indefinite in their recitation of the phrase "at least about 90% sequence identity" recited in claim 21, because the minimum sequence identity is not clear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A) Claims 20 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

i) Claims 20 and 23 are drawn to an isolated polypeptide having phosphohydrolase activity comprising an enzymatically active fragment of the amino acid of SEQ ID NO:6, and a composition thereof.

ii) Claims 22 and 23 are drawn to an isolated polypeptide having phosphohydrolase activity comprising an amino acid sequence encoded by a polynucleotide that hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO:5 or its complement, and a composition thereof.

iii) Claim 24 is drawn to the polypeptide according to any one of claims 19-22 that comprises amino acid residues 47-68, 123-138, 167-187 and 194-214 of SEQ ID NO:6.

i) The instant specification describes an isolated polypeptide having phosphohydrolase activity consisting of the amino acid sequence of SEQ ID NO:6, or the mature portion thereof. However, the instant disclosure of the amino acid sequence of SEQ ID NO:6, does not adequately describe the scope of the claimed fragments of said sequences, each of which encompasses a substantial variety of subgenera, for two reasons. First, Page 18 of the specification defines the term "fragment" as a stretch of amino acids of at least 5 amino acids long. It is noted that the specification does not describe a single fragment of at least 5 amino acids of SEQ ID NO:6, other than the mature protein from SEQ ID NO:6, wherein said fragment has phosphohydrolase activity. There is no description of the required structural and specific phosphohydrolase functional features encoded by the wide range of fragments encompassed by the instant claims, or of the conserved regions that would be critical for these features. Further, the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the fragments encompassed. Second, by use of comprising language, said fragments can also encompass an indeterminate number and type of additional nucleic acids, in addition to the minimum length of 5 amino acids.

It is noted that though the claimed invention is directed to polypeptides and not cDNA, the principle of the following still holds for said polypeptides: a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly&Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Therefore, there is inadequate written description of an isolated polypeptide having phosphohydrolase activity comprising an enzymatically active fragment of the amino acid of SEQ ID NO:6, and a composition thereof.

ii) Nor does the instant disclosure of the amino acid sequence of SEQ ID NO:6 adequately describe the scope of the claimed polypeptides having phosphohydrolase activity comprising an amino acid sequence encoded by a polynucleotide that hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO:5 or its complement,or a composition thereof, as recited in claims 22-23. However, by reciting hybridization language, said polypeptide can be of an indeterminate length (smaller or larger than SEQ ID NO:6) and also encompass an indeterminate number and combination of amino acid substitutions in SEQ ID NO:6. Since the applicants have not disclosed a single polypeptide having phosphohydrolase activity other than a polypeptide comprising an amino acid sequence 6 or the mature portion thereof, the invention encompassing said claimed polypeptide having phosphohydrolase activity comprising an amino acid sequence encoded by a polynucleotide that hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO:5 or its complement, or a composition thereof, is not adequately described along the lines of reasoning discussed in the previous paragraphs.

iii) Nor does the instant disclosure of the amino acid sequence of SEQ ID NO:6 adequately describe the scope of the claimed polypeptides that comprise amino acid residues 47-68, 123-138, 167-187 and 194-214 of SEQ ID NO:6, as recited in claim 24. It is noted that claim 24 does not include functional language when dependent on claim 19. Therefore, said polypeptides can be of an indeterminate length (smaller or larger that SEQ ID NO:6) and also encompass an indeterminate number and combination of amino acid additions and amino acid substitutions in SEQ ID NO:6, and amino acid residues 47-68, 123-138, 167-187 and 194-214 of SEQ ID NO:6 can be in any position of the polypeptide sequence and in any order. Since the applicants have not disclosed a single polypeptide that comprises amino acid residues 47-68, 123-138, 167-187 and 194-214 of SEQ ID NO:6, other than SEQ ID NO:6 itself, the invention encompassing said claimed polypeptides, is not adequately described along the lines of reasoning discussed in the previous paragraphs.

B) Claims 20 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

i) Claims 20 and 23 are drawn to an isolated polypeptide having phosphohydrolase activity comprising an enzymatically active fragment of the amino acid of SEQ ID NO:6, and a composition thereof.

ii) Claims 22 and 23 are drawn to an isolated polypeptide having phosphohydrolase activity comprising an amino acid sequence encoded by a polynucleotide that hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO:5 or its complement, and a composition thereof.

iii) Claim 24 is drawn to the polypeptide according to any one of claims 19-22 that comprises amino acid residues 47-68, 123-138, 167-187 and 194-214 of SEQ ID NO:6.

i) The instant specification discloses an isolated polynucleotide comprising a nucleotide sequence (SEQ ID NO:5), encoding an isolated polypeptide having phosphohydrolase activity consisting of the amino acid sequence of SEQ ID NO:6, or mature portion thereof. However, the instant specification does not provide adequate guidance and direction regarding how to make and use an isolated polypeptide having phosphohydrolase activity comprising any enzymatically active fragment of the amino acid of SEQ ID NO:6, as recited in claims 20 and 23. Page 18 of the specification defines the term "fragment" as a stretch of amino acids of at least 5 amino acids long. However, the specification does not disclose a single fragment of SEQ ID NO:6, other than the mature protein from SEQ ID NO:6, wherein said fragment has phosphohydrolase activity. Further, the prior art does not provide compensatory structural or correlative teachings to enable one of skill to predict which of the fragments encompassed by the instant claims will have phospohydrolase activity. Therefore, it would require undue experimentation for one of skill to predict which of said fragments will have phosphohydrolase activity.

Since the nucleic acid sequence of a polynucleotide determines its protein coding properties, predictability of which changes can be tolerated in a polynucleotide's nucleic acid sequence and still retain similar functions and properties requires a knowledge of, and guidance with regard to which nucleic acids in the nucleotide sequence, if any are tolerant of modification and which are conserved (ie., expectedly intolerant to modification), and detailed knowledge of the ways in which the product's structure relates to its functional usefulness. However, the problem of predicting functional aspects of the product in terms of what changes can be tolerated is complex and well outside the realm of routine experimentation. This complexity is due in part to the fact that the relationship between the amino acid sequence of a peptide (and its corresponding encoding nucleic acid sequence) and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo et al., (V), newly cited, in The Protein Folding Problem and Tertiary Structure Prediction,1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495). Therefore, there is no evidence of record to show that one skilled in the art would be able to practice the invention as claimed without an undue amount of experimentation.

Since the isolated polypeptide having phosphohydrolase activity recited in claims 20 and 23 comprises an enzymatically active fragment of the amino acid of SEQ ID NO:6, said fragments can also encompass an indeterminate number and type of additional amino acids, in addition to the minimum length of 5 amino acids in length from SEQ ID NO:6. Therefore it would require undue experimentation to make a fragment containing unspecified amino acids and predict which fragments have phosphohydrolase activity. It is noted that the smallest fragment of SEQ ID NO:6 disclosed to have phosphohydrolase activity is the mature portion of SEQ I DNO:6. . Therefore, it would require undue experimentation by one of skill in the art to predict A) the sequence of said fragments or B) the sequence of the additional amino acid residues that are to be included in the fragment.

ii) By reciting hybridization language in claims 22-23, the recited polypeptide having phosphohydrolase activity and comprising an amino acid sequence encoded by a polynucleotide

that hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO:5 or its complement, can be of an indeterminate length (smaller or larger than SEQ ID NO:6) and also encompass an indeterminate number and combination of amino acid substitutions in SEQ ID NO:6. Since the applicants have not disclosed a single polypeptide having phosphohydrolase activity comprising an amino acid sequence encoded by a polynucleotide that hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO:5 or its complement, other than a polypeptide comprising an amino acid sequence 6 or the mature portion thereof, and the prior art does not teach any said molecule, and since further the prior art and the instant disclosure do not provide compensatory structural or correlative teachings to enable one of skill to predict which of the polypeptides encompassed by the instant claims will have phospohydrolase activity, it would require undue experimentation for one of skill to predict which polypeptide phosphohydrolase activity comprising an amino acid sequence encoded by a polynucleotide that hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO:5 or its complement, without further guidance from the specification.

iii) Other than SEQ ID NO:6 and the mature portion thereof, the specification does not disclose claimed polypeptides that comprise amino acid residues 47-68, 123-138, 167-187 and 194-214 of SEQ ID NO:6, as recited in claim 24. It is noted that claim 24 does not include functional language when dependent on claim 19, and therefore, function is not a limiting factor in the breadth of the claims. Therefore, said polypeptides can have any function, be of an indeterminate length (smaller or larger that SEQ ID NO:6) and also encompass an indeterminate number and combination of additional amino acids and amino acid substitutions in SEQ ID NO:6, and further, amino acid residues 47-68, 123-138, 167-187 and 194-214 of SEQ ID NO:6 can be in any position of the polypeptide sequence and in any order. Therefore it would require undue experimentation to make and use the breadth of said polypeptides without further guidance and direction from the specification.

C) Claim 24 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 24 is not supported by the specification or by the claims as originally filed. There is no support in the specification or claims as originally filed for the recitation "the polypeptide according to any one of claims 19-22 that comprises amino acid residues 47-68, 123-138, 167-187 and 194-214 of SEQ ID NO:6 ". There is no written description of the claimed invention in the specification or claims as originally filed. Thus the claimed invention constitutes new matter. It is noted that there is support in the specification and in the claims as originally filed for "the polypeptide according to any one of claims 19-22 that comprises amino acid residues 47-68, 123-138, 167-187 **OR** 194-214 of SEQ ID NO:6 ", (emphasis added). Applicant is invited to point out support for claim 24.

Allowable Subject Matter

Claim 19 contains allowable subject matter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 8:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305-3014 for regular communications and 703 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Amy DeCloux, Ph.D.
Patent Examiner,
January 11, 2003

Patrick J. Nolan, Ph.D.
Primary Patent Examiner,
Group 1640

Application No.: 09/905,744

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: Sequences which lack SEQ ID NO: tags are disclosed throughout the specification, including pagess 95, 98, 100, 101 and 103.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An *initial* or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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